THE AMERICAN JOURNAL
...OF...
OPHTHALMOLOGY.

VOL. XVI. FEBRUARY, 1899. NO. 2.

ORIGINAL ARTICLES.

PROFUSE HÆMORRHAGE SUBSEQUENT TO THE EXTRACTION OF SENILE CATARACT.[1]

BY B. E. FRYER, M.D., KANSAS CITY, MO.

PROBABLY there is nothing which can happen to the ophthalmic surgeon more appalling than profuse hæmorrhage following the extraction of senile cataract. There are no indications, no premonitions which enable us to prognose that this or that case will or will not be free from this dreadful disaster. We must theorize, I believe, if we consider the hydraulic factors plus the defective and diseased intra-ocular blood vessels almost always existent with senile cataract, that hæmorrhage may occur in any case. It has been my experience to meet with three instances in which abundant hæmorrhage occurred after very smooth extraction; two of these were published, and they are referred to among forty-eight others in Spalding's admirable paper on the subject in *Knapp's Archives of Ophthalmology*, Vol. XXV, No 1.

In this paper I propose to report a third case and to comment upon it and upon some of the views held by those who have been so unfortunate as to have this terrible result occur in their practice.

Mrs. S., aged 74 years, American, consulted me in July,

[1]Read at the Fourth Annual Meeting of the Western Ophthalmological and Oto-Laryngological Association, held at New Orleans, La., February 10-11, 1899.

1897, in regard to her right eye. I found she had incipient cataract, and that the tension was + 1. Vision sufficient to enable her to get about with caution. Visual field good. The left eye was simply a stump, sight in it had been suddenly lost about two years previously. Any attempt to ascertain the exact cause of the destruction of the left eye was not either very satisfactory or successful. All that I could discover was that the vision failed suddenly preceded by great pain and afterwards the globe shrunk to about half the normal size. My opinion is that there had been hemorrhagic glaucoma. As to general health all inquiry for any defects failed. No rheumatism, no gout, no specific complication; and the general appearance was that of good health and fair nutrition.

I at once began the instillations of pilocarpine for the right eye, and in a few days did an iridectomy upwards. These measures brought tension down and the case was kept under observation a year. In the meantime the cataract reached maturity and the operation was done. The eye was carefully prepared antiseptically with protargol for several days, cocaine anæsthesia was had, and the patient placed in Knapp's operating chair. The incision, which was wholly within the cornea, was made very smoothly, included a little more than two-fifths of that membrane. The patient was perfectly quiescent. No pressure was made upon the eyeball or lids, the latter being held apart by lid-retractors in the hands of my most skillful assistant, Dr. J. S. Lichtenberg. The lens was delivered very easily after a T-shaped capsulotomy. There was no collapse of the cornea; the edges of the incision were coaptated perfectly; the iris was in no way interfered with, and no portion of it became engaged in the wound. No vitreous was lost. The operation, which did not last longer than forty seconds, was finished at 11:45 A.M., and the eye carefully dressed, and absolute quiet enjoined. Previous to the operation I informed the patient's daughter that hæmorrhage was possible. Four hours after the operation, viz., at 4 P.M., I was hurriedly sent for, and on reaching the patient, found blood streaming down the face under the dressings, which latter were thoroughly saturated. The dressings were removed, the face and lid carefully cleansed with carbolic acid solution and sublimate gauze reapplied. Slight oozing continued, however, for eight or ten hours afterwards. The blood, I was informed by the patient's

daughter, had appeared very suddenly and in quantity. No vascular tissue was cut in the operation, and there was not the slightest stain of blood when the original dressings were put in place; this dressing consisted of six thicknesses of sublimate gauze held in place by strips of isinglass plaster. The case was closely watched by me for more than an hour after the first dressing was applied and no bleeding occurred, and the patient's daughter is very positive that the hæmorrhage did not take place until four hours after the operation was over, and when it appeared, it was with a gush and it continued as above mentioned. The eye became a stump but enucleation was not done.

Reflecting on this case, it seems that the unfortunate result was unavoidable. Every precaution was had to prevent it. The operation was perfectly smooth and regular in every respect. No pressure or traction was made upon the eyeball by any of the instruments. The most thorough quiet was enjoined upon the patient. I watched the case closely for an hour after the extraction and for three hours after that there was no bleeding. No drug was given having for its object prevention of the hæmorrhage, believing as I do that any remedy heretofore suggested, is futile. Possibly a thoroughly and long quieting dose of morphia might have been tried, but the nauseating and vomiting effect of this might have produced the result which it was so desirable to avoid.

Spalding's paper, in *Knapp's Archives of Ophthalmology*, which I have alluded to, reports a hæmorrhage after cataract extraction, and gives the bibliography of fifty others. Spalding says: "This accident is supposed to be extremely rare, and many ophthalmic surgeons with whom I have conversed, had never heard of but one or two cases of the sort, and they expressed surprise when I mentioned that I had discovered as many as fifty reported cases, whilst of the unreported (owing to a sense of shame perhaps) there must be a much larger number than we have at present any idea."

Spalding comments on his own case and gives in more or less detail an abstract of a "few of the most important cases reported especially of those in which the authors express some opinion in regard to the etiology of the accident, or concerning some means for prevention."

I shall quote from Spalding's paper extensively with ref-

erence to the opinions of the writers which he embodies in his essay. And I desire here to give him full credit for his valuable presentation of these, exhibiting as they do the views of many of the prominent ophthalmologists throughout the world on this important but neglected subject.

With reference to his own case Spalding states, that he believes the hæmorrhage is due to the relaxation of the suspensory ligament permitting the too rapid extraction of the lens, as a result of which the degenerated vessels in the region of the incision give way. While this may explain somewhat bleeding which immediately follows the extraction, it scarcely does so where the bleeding is delayed until several hours afterwards. In this latter condition it is more probable that fluctuations of pressure made by the lids upon the eyeball produce a partial emptying of the anterior chamber from time to time, with the result of diminished and varied support of the vascular walls with finally a rupture of one or more of the vessels. While in the former, where the bleeding occurs as really a part of the operation the one diminution of supporting pressure is sufficient to cause the break.

Hirschberg (*Centralblt. f. Augenheilk.*, 1890, p. 538), who reviews Wood's paper in the *New York Medical Record*, May, 1890, asks, when glaucoma complicates senile cataract, whether we shall first iridectomize and then extract, or to perform both operations at the same sitting. Hirschberg adds, prophylaxis is useless, as there are no premonitory symptoms. (Spalding). This corresponds with my own views.

Fage (*Arch. d'Ophth.*, August, 1889) reports a case where the microscopic examination demonstrated that the hæmorrhage came from between the choroid and sclera. Fage adds, that if he had to extract from one eye where its fellow had been lost from hæmorrhage, he would use ergotine treatment preliminary to the extraction, and insist upon perfect quiescence of the patient after operation. (Spalding).

I would emphasize here, in reference to this suggestion as to the use of ergotine which is made by Fage and others, both in this country and in Europe, that the remedy would add to, rather than diminish, the risk of hæmorrhage; for those who recommend ergotine lose sight of the fact, that while the drug will produce as the essential effect diminution of vessel-calibre, it follows with this, that there will also be a correspond-

ing increase in systemic arterial pressure, which effect being the one we should seek to avoid, not only as regards the ocular vessels, but those of the brain With increased arterial tension, even though we have diminished vessel-calibre, it can be readily seen that the risk of rupture of the vascular walls is the greater. In 1884, at the French Society of Oculists, this subject being under discussion, ergotine was also suggested as a prophylactic.

De Schweinitz (*Annals of Ophthalmology and Otology*, III, p. 12) reports a case with but one useful eye. De Schweinitz properly took the precaution to do a preliminary iridectomy. A month afterwards, on completion of the corneal incision, a bead of vitreous appeared and the lens was immediately removed with the spoon. After the bandage was applied the patient complained of severe pain in the eye, and of nausea. Anticipating hæmorrhage, a hypodermatic injection of morphia was given, and the patient placed in a sitting position, but hæmorrhage came and the eye collapsed. (Spalding).

Galezowsky has stated that he had had but one hæmorrhage in over 1900 simple extractions, and believes that rarity of the bleeding in his cases is due to the fact that in simple extraction atheromatous vessels in the vicinity of the iris are not opened. This assertion, however, is void, because in the case of de Schweinitz and in my last case a preliminary iridectomy was done sometime prior to the extraction.

Moreover, Knapp, whose skill as an operator is so universally acknowledged, met with a case of his own, after simple extraction. Knapp is of the opinion that the bleeding came from the anterior portion of the choroid.

Fage examined an enucleated eye which was removed for hæmorrhage following extraction, and states that the blood came from the anterior portion of the choroid; both the retina and choroid were detached.

A number of other ophthalmologists have reported cases, while in a few of them the bleeding occurred a few hours after the operation, as in my case and in de Schweinitz's, in the majority of instances the blood appeared either during the operation or just after. The opinion of the majority of the reporters, as to the site of the vessels from whence the bleeding came, is that it was from the uveal tract—either the ciliary body or the choroid. A number of other writers might be

quoted, but as their views are in the main similar to those already given, they may be omitted. Some she more prominent are Knapp, Gruening, Risley, Jackson and H. Derby in this country, and Mooren, Lebrun, Dufour, Darier, Simi and others abroad.

In summarizing I believe it correct to state:

1. That profuse hæmorrhage, after senile cataract extraction, is not so rare an occurrence as has been supposed; that it may follow the most smooth operation; that it can take place when the extraction is simple as readily as when the operation includes an iridectomy; that even with the precaution of a preliminary iridectomy the catastrophy may happen.

2. That while the bleeding may follow any cataract extraction, it is more likely to do so in cases in which glaucoma exists or has existed; that there are no means of prognosing as to its occurrence or absence in any case.

3. That there are no certain means known of preventing the hæmorrhage, and that the suggestion as to the use of ergotine for prophylaxis is erroneous and perhaps dangerous. If an opiate for prevention of the accident is used the patient should be kept narcotized more or less, until the healing of the incision is assured. But in that event a preliminary test should be made upon the patient as to the effect of the drug upon him so as to enable the operator to decide as to the safety of exhibiting the narcotic at the time of operating.

4. The maturity or immaturity of the cataract plays no part as to causation.

PAMPHLETS RECEIVED.

"The Sequelæ of Middle-Ear Suppuration," by E. B. Dench, M.D.

"On Traumatic Recurrent Corneal Neuralgia," by B. Wicherkiewicz, M.D.

"The Scientific Borderline Between Sanity and Insanity," by E. C. Runge, M.D.

"Diseases of the Alimentary Canal,—Treatment, Etc.," by J. O. DeCourcy, M.D.

ON THE PATHOLOGY OF CATARACT, ESPECIALLY IN ITS EARLIEST STAGES.[1]

BY ADOLF ALT, M.D., ST. LOUIS, MO.

[WITH MICRO-PHOTOGRAPHS.]

IN my text-book on "The Normal and Pathological Histology of the Human Eye," published in this country in 1880 under the title of "Lectures on the Human Eye," and in the chapter on "The Crystalline Lens," I stated it to be my opinion that "the pathological changes of the crystalline lens, when the capsule is intact, and which are called cataract, are simply regressive metamorphoses of the elements constituting the lens." To this standpoint my then comparatively limited studies seemed to force me. I had then never had occasion to see anything in lenses with an intact capsule like the hyperplasia and proliferation of the capsular epithelial cells as Iwanoff and Becker had described it under the term phakitis. And I may add right here, that even to this day it has not been my good fortune in the many cases of cataract which I have now examined, to see certain typical forms of phakitis as drawn and described by Becker. This discrepancy may, however, probably be explained by the difference in the material for examination which we each had at our disposal. The large vesicular cells as described by Wedl, Iwanoff and Becker I have in those days mistaken for drops and globules of myeline (liquor Morgagni) which, as I now know, was due to my insufficient staining methods which did not make their nucleus visible.

Becker took immediate occasion to criticise my whole description very severely, but surely only in part justly, as will be clear after my further statements.

Three years after my book he published his excellent, exhaustive and magnificently illustrated book on "The Crystalline Lens in Health and Disease." The study of which not

[1]Read at the Fourth Annual Meeting of the Western Ophthalmological and Oto-Laryngological Association, held at New Orleans, La., February 10-11, 1899

only showed me wherein I had held an incorrect opinion, but also prompted me to examine all cataractous lenses within the intact capsule which I could obtain with especial care.

This material, and through it my experience, has now gradually grown far enough that I think it appropriate and just to myself to make it known to you and others interested in this subject, especially since I can not only add my testimony, as far as it goes, to Becker's statements, but think that I am in a position to fill some gaps in his description, particularly as concerns the earliest stages of cataract formation.

The discrepancies which still exist between our opinions, as I stated before, are probably in part accounted for by the fact, that Becker seems to have made his studies chiefly on ripe and over-ripe cataractous lenses which were furnished him by Pagenstecher and others whose method was to extract cataracts with their capsule. On the other hand, my studies since 1880 have chiefly been made on cataractous lenses in the earliest and earlier stages of the development of cataract as I found them in eyeballs removed on account of tumors in the orbit and neighborhood, or affecting the eyeball itself, on account of glaucoma, or cyclitic processes, and finally on eyeballs taken from dead subjects. Traumatic cataracts due to a ruptured lens-capsule are here not considered.

From Becker's severe criticism of my statement that cataract was a *regressive* metamorphosis, I had expected that his researches had taught him that cataract, on the contrary, must rather be considered as a *progressive, proliferating*, so to speak *inflammatory* process. I found, however, after all, that in his book he declared the beginning of the formation of a cataract to be due to the continued and excessive sclerosing process of the nucleus of the lens, but that, secondarily, this leads to the changes which Becker considers as active processes. In this fundamental point, then, our views were not as widely apart from each other as from his criticism it had appeared.

Permit me to recall to you here in a condensed form what Becker found in cataractous lenses.

The sclerosing process of the nucleus of the lens, which is a physiological retrogressive process, leads gradually to the formation of fissures between it and the cortex which may even sometimes be seen ophthalmoscopically. Gradually a more and more distinct separation between cortex and nucleus

may be observed. The outline of the yellow clear nucleus is sharply defined from the glass-like, clear cortex. Further on cloud- and point-like opacities appear in the cortex and increase in numbers. They may in rarer instances, also, be seen in the outermost layers of the nucleus. At this period the lens usually takes up fluid from without by imbibition and increases in volume. After a varying time this fluid is again given off and the lens resumes its normal volume. Diffuse and localized opacities in the nucleus Becker never saw, contrary to Foerster. Now abnormal chemical processes take place within the lens due to the stagnation of the imbibed fluid within the fissures separating the lens-fibers, whether these are preformed or due to the sclerosis of the nucleus. The fact, found by Priestley Smith, that cataractous lenses are of smaller volume than clear lenses of the same age, Becker lays great stress on, as a proof that the formation of fissures is due to an excessive sclerosis, an excessive *physiological retrogressive* metamorphosis of the lens.

The altered conditions of diffusion lead next to the formation of round- and drop-like bodies within the fissures, presenting in their aggregation the appearance of algæ or bamboo-joints and having a double contour. Becker calls them coagulated albumen and is not sure whether the coagulation took place *intra vitam* or is due to death or the influence of the hardening fluids in which the specimen was preserved. The description of these masses corresponds with the appearance of what is usually termed myeline (or liquor Morgagni) and represents the softer, semi-fluid contents of the lens-fibers. Then the neighboring fibers are changed into a condition of molecular opacity (fatty degeneration) and finally larger droplets are formed and the lens-fibers appear wrinkled. From the similar gradually progressing destruction of more and more fibers a grumous mass results which consists of detritus, globules of albumen (liquor Morgagni) and fat, and which sometimes contains granules of lime and crystals of cholesterine. This, according to Becker, is the way in which a senile cataract forms and progresses. The only juvenile cataract which he had occasion to examine was from a diabetic subject. The most characteristic change was a large quantity of a clear fluid of less refraction than the lens-fibers which at the æquator had penetrated, according to his opinion, through the capsule from

without. It filled numerous spaces between the lens-fibers. Gradually the lens-fibers swell and disintegrate in a similar manner as is the case in senile cataracts.

Thus far, you see, Becker speaks only of regressive changes, which evidently are sufficient to cause and lead to what we call a ripe cataract. This description does not differ much in essential points from what I had described. However, by far the larger part of the descriptive portion of Becker's book is devoted to the evidently secondary changes in the fibers of the

FIG. 1.

cortex, the capsular epithelial cells and the young lens-fibers at and near the æquator, which he partly considers as degenerative, partly as active processes. In the cataractous lenses which he examined these changes were nearly always present. They are undoubtedly well known to you, as their description can now be found in every text-book.

To the foregoing description of the formation of a cataract, from which in the main I see no reason to differ, I wish to add now the description of what further I have found in my researches.

In old lenses in which no formation of cataract was suspected I have frequently come across small spaces, lentil-shaped in meridional and round in æquatorial sections, and larger fissures lying between the lens-fibers usually concentrically arranged around the nucleus. These spaces and fissures are *intra vitam* probably filled with the nutritive fluids which pass through the lens. Sometimes such fissures take on an eccentric course and break through different fiber-layers. Further, there are always drops of myeline, especially in the sutures.

In some lenses I found no other changes, but a number of larger and smaller fissures near the æquator inside the posterior capsule. These were filled with a drop-like material, slightly granular, with a higher magnifying power. The picture it produced was very much like what Becker calls coagulated albumen in the shape of aigæ or bamboo-joints. I take this substance to be myeline and its occurrence in such a large quantity to be the first sign of the breaking down of the lens-fibers in which fluid imbibed from the outside through the capsule probably plays an important part. (Fig. 1).

From a larger number of lenses showing in addition what I consider to be the first signs of a beginning cataract, allow me to select a few for a more detailed description. I want to state first that of all these lenses I have the whole series of sections either in a meridional or æquatorial direction, and that what I have seen covers all the changes in such a lens which our present means could render visible.

In an eyeball, removed from an old lady on account of a carcinoma, a general haziness of the lens had been observed *intra vitam.*

I found the nucleus to be so large that the cortex at the anterior and posterior poles formed but a thin band. At the æquator the cortex was naturally thicker. The capsular epithelial cells were normal in appearance throughout and showed no irregularity in their arrangement in any of the sections.

Besides a number of concentric fissures at the æquator, there was in this region just inside of the nucleus a large irregular cleft, differing greatly in width and having an eccentric course, so as to pass through numerous fiber-layers. It contained a granular substance (fatty detritus ?). (Fig. 2). Deep within the nucleus there were a number of broad lines, forming some concentric, some totally eccentric, curves and double bends, which

appeared as fissures, but are simply produced by numerous small dots which have taken on a deep blue stain with hæmatoxyline. Aside from these the outer layers and especially the posterior ones of the nucleus are dotted throughout with these same blue spots. They are larger in the peripheral than in the more central layers. Even with immersion lenses no structure can be made out in them; they appear, however, slightly granular. I consider these dots as the product of some chemical substance formed at the very beginning of the fiber destruction, which has a particular affinity for hæmatoxyline. Eosine does not stain them.

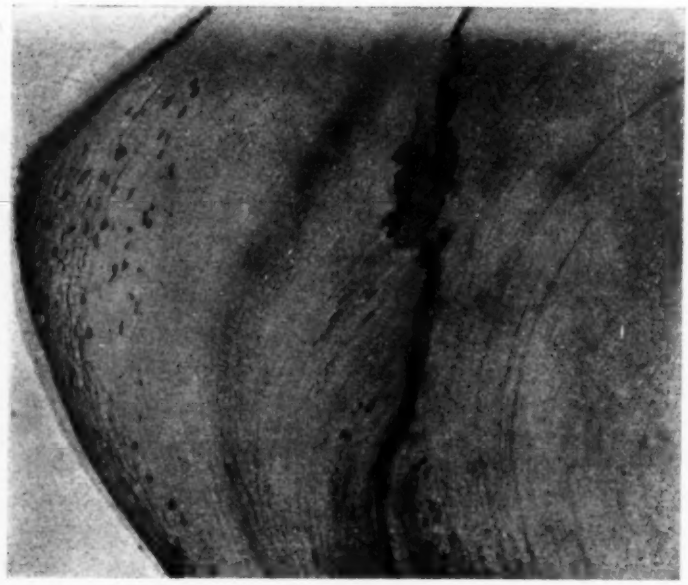

FIG. 2.

Behind the æquator the young lens-fibers just inside the capsule appear partly filled with and partly pressed asunder by a light transparent fluid material which stains with eosine slightly, but not with hæmatoxyline. It looks very much like what Becker described in the juvenile cataract. The lens-fibers here are evidently beginning to undergo a regressive metamorphosis.

The two eyes, taken from a dead body, had *intra vitam* both shown macroscopically visible striæ. I cut both into

æquatorial sections. They seem to represent stages of cataract formation just a little farther advanced than the previous one.

In the right eye the cortex and capsular epithelium were perfectly normal in appearance. The nucleus, however, to its very center was dotted with millions of dark-blue spots of varying size, largest and very large at its anterior and posterior surfaces. These dots in the æquatorial sections were in places arranged in lines forming radii. In one section I counted thirteen such radii. These start at some distance inward from the capsule and run toward the center. In several sections some of them meet here and form an irregular star. Some few concentric fissures which contain myeline drops lie in the periphery. (Fig. 3).

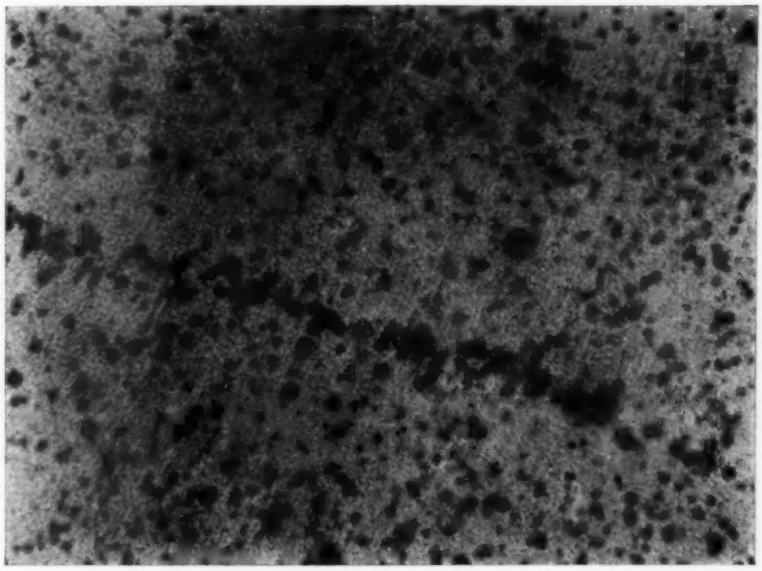

FIG. 3.

In the left lens the cortex appeared broader and not as firm, but not altered so far that its elements could not be recognized. The peripheral layers of the nucleus were dotted with innumerable dark blue spots of varying sizes, not, however, as large as in the other eye. They were largest near the posterior surface of the nucleus. In this lens, too, these dots formed a number of radius-like lines, which starting at some distance

from the capsule, ran inwards towards the center. In some sections I counted ten such radii.

These dotted radii evidently correspond to the radii of the lens star and are the histological substratum for the striæ macroscopically seen during life.

Aside from these larger dots innumerable smaller ones lie in the cementing substance between the lens-fibers and thus outline the fibers beautifully. (Fig. 4).

FIG. 4.

The capsular epithelium is everywhere normal, excepting at the peripheral terminus of one suture. Here a larger amount of myeline lies in the place of degenerated lens-fibers and the formation of vesicular cells has begun.

In another eye, removed from an old man on account of a conjunctival sarcoma, the lens had *intra vitam* been quite hazy, but no striæ were visible. In this lens the capsular epithelial cells were perfectly normal. Aside from a few fissures I found nothing abnormal excepting again innumerable small spots stained dark blue with hæmatoxyline which were distributed throughout the lens, leaving but the most peripheral layers of the cortex free. In this lens, as in the first one here described, these dots nowhere formed radii.

Only at the peripheral termini of the lens sutures larger and smaller drops of myeline took the places of degenerated lens-fibers and in these places some vesicular cells had been formed.

Without going further in this detailed description of lenses being in a similarly early stage of cataract formation, I may here sum up, that evidently the sclerosis and death of the lens-fibers cause, first, the formation of fissures between the fibers, then the destruction of the outer parts of the fibers probably aided by imbibition of fluid which sets their contents free in the shape of myeline drops. At the sa ne time certain chemical substances result from this tissue death which by the staining with hæmatoxyline become visible as dark-blue spots. While these spots may appear in almost all the parts of the lens-tissue except the epithelial layer, they appear most numerous and largest near the posterior surface. These same chemical substances may be more especially located in the seams of the lens-fibers and thus form radius-like lines, which seem to be the earliest histological substratum for the striæ seen macroscopically *intra vitam*.

That various abnormal chemical combinations are produced during cataract formation is very evident from the peculiar manner with which such lenses take up the different stains. While some parts are evidently acidophile others are decidedly basophile, as is undoubtedly well known to every one who has paid some attention to this subject.

The chemical substance here referred to possibly and perhaps probably may act as an irritating toxine on the capsular epithelial cells and on the younger æquatorial lens-fibers and thus perhaps stimulate them to the changes later on observed within them.

That this substance, whatever its character, is later on diffused, or at least that it is later on formed in a more general way, is evident by the fact that at later stages these small dots are no longer seen, while, however, large portions of the lens take up the hæmatoxyline stain much more eagerly than others.

The diffusion or more general generation of this substance seems to usher in the further disintegration of lens-fibers, as well as the changes in the capsular epithelial cells and the younger lens-fibers.

Of such changes consecutive and secondary to the degeneration and regressive metamorphosis of the older lens-fibers I have seen the following.

I have never seen the typical cell nodules formed by a proliferation and hyperplasia of the capsular epithelial cells as Becker has described them as atrophic hyperplasia. He found them especially around so-called colloid deposits on the inner surface of the anterior lens-capsule.

I have seen, however, in a number of lenses that the proliferation of the capsular epithelial cells had led to a duplication and triplication of this layer. In one case I found numerous rows of cells growing from this layer into fissures between the neighboring degenerating lens-fibers.

In quite a number of cases, especially of consecutive cataracts, I found lying close to the anterior capsule, which in these cases always was wrinkled, a tissue closely resembling connective tissue and with a lamellar arrangement very similar to the cornea. As in these cases the capsule was intact, it is more than probable that this strange tissue had been produced by an abnormal process from the anterior capsular epithelial cells, which are wanting in such cases. I have had occasion to describe a similar tissue as formed by the endothelium on Descemet's membrane (AMERICAN JOURNAL OF OPHTHALMOLOGY, April, 1896), the cells of which are identical with the anterior capsular epithelial cells as regards their shape, arrangement and general behavior, if they are not of the same origin. Such newformed lamellar tissue was also described by myself (Lectures on the Human Eye) and later by Becker and Collins (*Ophthalmic Review*) as found in the cone of anterior polar cataracts. It has also been produced experimentally by Leber and corresponds to what Becker calls the true capsular cataract. In one lens I found the amount of this tissue so great that I have a suspicion that at some time the lens-capsule had been wounded, although I could find no other evidence to support this suspicion. Enclosed between its lamellæ were here and there small rows of cells evidently derived from the capsular epithelium and surrounded by a small quantity of myeline, probably formed by these cells.

In a number of cases I have seen a partial or total lining of the posterior lens-capsule with newformed epithelial cells, a few times even in cataracts which were otherwise but little ad-

vanced. Becker calls these newformed epithelial cells on the posterior capsule pseudo-epithelium. According to him, they are derived from the anterior capsular epithelial cells which, when the æquatorial young fibers are destroyed, find themselves freed from their opposition and grow backwards along the inner surface of the capsule. I, also, have specimens which seem to prove the correctness of this opinion. Yet, the question remains open, why this backward growth of the anterior epithelial cells does not happen more often in cases of cataract. When this newly-formed epithelium lines the whole of the

FIG. 5.

posterior lens-capsule it appears very much like that of the anterior capsule. Yet, its cells are usually flatter and their nucleus appears more oval; sometimes also a cell is found with an enormous round nucleus. Frequently small portions are free from epithelium and then the arrangement of cells is naturally not as regular as on the anterior lens-capsule.

The lack of opposition from the normal contents of the lens, due to the sclerosis, formation of fissures and destruction of the lens-fibers, especially at the æquator, is, according to

Becker, the first cause, also, of certain changes in the young æquatorial lens-fibers and the epithelial cells which lead to the formation of the now well known spindle-shaped enlargements and vesicular cells. I am inclined to think that other factors help in producing these cells among which again the imbibition of the fluids from without is one of the most active.

I have had occasion to study these processes in their earliest beginning.

FIG. 6.

In a lens otherwise almost normal and presenting but a few fissures and in which there was particularly no alteration in the capsular epithelium, I found that some of the youngest lens-fibers at the æquator had lost their regular outline and had become slightly wavy. Others looked as if they were getting liquefied and spreading in parts. (Fig. 5). Here and there a nucleus was seen changed from its normal oval shape to a round one, was surrounded by a light, round area of a material which did not take on any stain from hæmatoxyline, but a slight tint from eosine. Around some nuclei this area had grown considerably. As this process goes on, whether it is due to a degenerative process within the fiber alone or in combination with the

imbibition of fluid material from the neighborhood, the well-known round, oblong and spindle-shaped enlargements of the

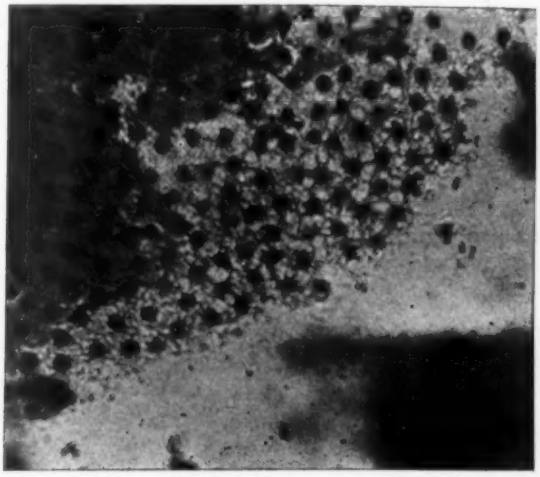

FIG. 7.

FIG. 8.

fibers are formed. That they grow at the expense of the neighboring fibers which atrophy is especially well seen in æquatorial sections. (Fig. 6).

In a similar manner the vesicular cells, which sometimes

obtain an enormous size, are formed from the capsular epithelium, especially near the æquator. In a number of lenses I have found the lens-fibers at the peripheral termini of the sutures totally destroyed and their myeline free in the shape of drops and globules. In every one of these lenses I found that the neighboring capsular epithelial cells had assumed the star- or spider-like shape, which I have described as the condition of unrest due to an irritant as observed in Descemet's endothelium (AMERICAN JOURNAL OF OPHTHALMOLOGY, February, 1896). This protoplasm, instead of having the normal hexago-

FIG. 9.

nal shape, is in an irregular manner in parts contracted towards the nucleus, leaving but a few thin prolongations by which the neighboring cells touch each other, with open spaces between them, through which I think the fluids from the outside can more rapidly pass into the lens-tissue. (Fig. 7).

Among these cells a number of nuclei are seen to be surrounded by a light area, which is larger than a normal cell and acts when stained with hæmatoxyline and eosine like the one just described in the young lens-fibers. The nucleus of such a swollen cell is usually smaller than that of the surrounding cells.

(Fig. 8). Gradually, as the neighboring lens-fibers disintegrate more and more, this light area increases in size and thus these cells grow larger and larger, living, so to speak, on the fat of the land. That, at first at least, these vesicular cells are not simply cells which are undergoing a hyaline, colloid or dropsical metamorphosis,seems to be probable on account of the existence of two and three nuclei in some of them, unless this is brought about by an early coalescence of neighboring cells. (Fig. 9). The neighboring epithelial cells may remain for a time apparently intact or join in the process of vesicular swelling, or they

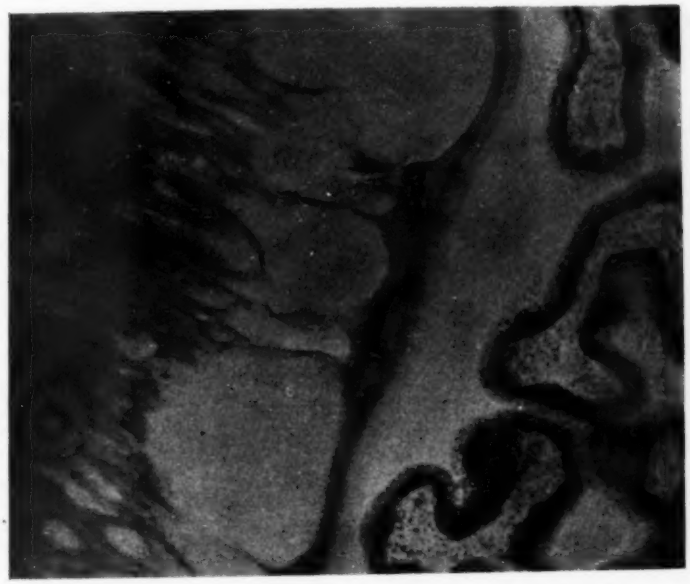

FIG. 10.

disappear by atrophy from pressure. Finally death overtakes the vesicular cells, also, their nuclei disappear and neighboring cells coalesce with each other. In this way smaller and larger cavities may be formed which contain a coagulable substance which takes on a slight stain with eosine. The is probably the way in which a Morgagnian cataract begins to form. (Fig. 10).

The course of the formation of a cataract from the foregoing seems to be: First, excessive physiological regressive shrinkage, called sclerosis, of the nucleus, causing smaller and larger fissures to appear between the lens-fibers. Then imbi-

bition of lens-fibers with fluids from the outside, aiding in the destruction of these fibers, more especially at the æquatorial terminus of the seams. The formation of chemical substances which may act as irritants on the younger fibers and the capsular epithelium. The formation of spindle-shaped swellings in the lens-fibers and of vesicular cells in the epithelial layer, especially near the æquator, which seems to be enhanced, if not directly caused, by imbibition of fluid from the outside which is at first located around the nucleus of the fibers or cells. Such an imbibition is made easier by the peculiar change in the epithelial cells described above by means of which numerous minute portions of the lens-capsule become devoid of their protoplasmic lining. Further imbibition and the growth and confluence of vesicular cells may then lead to the formation of large cavities filled with the fluid these cells contained, and thus to the formation of a Morgagnian cataract may begin. Incidentally, further proliferating changes may occur in the capsular epithelial layers, as the newformation of epithelial cells in larger nodules (Becker) or forming several parallel layers, or leading to an epithelial lining of the posterior capsule, or, finally producing a peculiar lamellar tissue which very much resembles connective tissue on the inner side of the anterior lens-capsule.

To these may later be added further products of regressive metamorphosis as deposits of lime, crystals of fat acids and cholesterine, etc.

ASTIGMATISM ACQUIRED BY A CHANGE IN THE CURVATURE OF THE CORNEA.

BY SWAN M. BURNETT, M.D., PH.D., WASHINGTON, D. C.

IT has been generally agreed that regular astigmatism is due, in the main, to a faulty curve in the corneal surface, and that it is congenital and permanent. To the first proposition there are quite a number of exceptions, as the use of the the ophthalmometer has taught us. We now know that there is a normal and almost uniform amount (about 0.5 D. and "against the rule") of astigmatism, referable to the lens, and that in some instances it has been very considerably more.

The second proposition has been much more universally accepted and it has even been questioned whether there are any genuine deviations from the rule, except in cases of traumatism. It is true a number of cases have been placed on record and by very accurate observers, showing a development or increase in astigmatism from year to year, and particularly in the early periods of life, but in such reported cases as have come under my notice, it has been nothing more, apparently, than the becoming manifest of an astigmatism held latent by some action of the accommodation. There seems to be no doubt that with increasing age and almost *pari passu* with loss of accommodative power, an astigmatism may become apparent which was not manifest before, even under the influence of a cycloplegic agent.

At the last meeting of the American Medical Association in Denver (1898) the question was under discussion in the section of ophthalmology, and several members gave experiences with an increase of astigmatism in their own eyes. Thus, Dr. G. C. Savage had noted an increase from — 0.5 to — 2.25 axis vertical. The ophthalmometric measurements when he was examined by that instrument gave the last amount of astigmatism, and it has remained, subjectively, at the same for the last nine years. Dr. Edward Jackson, whose careful work in this department we are all familiar with, has found his astigmatism, under a mydriatic, increase from 0.5 in one eye, and 0.75 in the other, to 1.75 and 2, respectively. He did not give the measurement of the ophthalmometer in his case. Other members reported like experiences either in their own persons or in their patients. Javal also noticed the evolution of an astigmatism with increasing years.

Most of these men are of the opinion that the development of the astigmatism was due to a change in the lens, and most of them think it caused by an alteration in its position. The influence of a partial action of the ciliary muscle has also its supporters. It seems rather remarkable that, though the ophthalmometer has been in very general use in this country now for a number of years, no case has been brought to notice, which I remember to have seen, where a marked and permanent change took place in the corneal astigmatism independent of a traumatism. Some instances of change in the cornea due to pressure of a chalazion have been reported, but the astig-

matism has disappeared on removal of the growth. My own use of the ophthalmometer dates back to 1885, and I examine every patient by this method that applies with any but acute inflammatory trouble. Many patients naturally come back for a change of glasses, re-examination, etc., and in every such instance another examination with the ophthalmometer is made. I have noted from time to time slight discrepancies in in the result of these different examinations, often amounting to 0.5 D. or even more, but have always been inclined to put them down to a fault in observation, since it is easy to commit such an error, particularly with the varying light of day, which is what I use in my ophthalmometric examinations. In the following case, however, the change is so marked that I deem it worthy of being placed on record as a contribution to the study of the question in hand.

Miss Helen S. was first brought to me on January 23, 1893, when she was 12 years old, to be treated for an attack of subacute conjunctivitis. She had then V. = $^{5}/_{IX}$ in both eyes. The shadow-test revealed a small amount (— 0.5 D.) of astigmatism according to the rule in both, but this glass gave no material improvement in vision. The ophthalmometer gave R. 180° $45^{1}/_{2}$ with a crossing of the mires of 1 D. at 90°; L. 180° $45^{1}/_{2}$ 90° × 0.5 D. It would appear from the record that she paid me several visits and there seems to be no reason to suppose I did not exercise my usual care in the various examinations. The conjunctivitis subsided and no glasses were ordered.

Within the last two or three years, however, she has noted a gradual failing in the distant vision of the right eye particularly. On November 25, 1898—that is nearly six years after the first examination—she again presented herself for treatment. The condition then was as follows:

R. V. = $^{5}/_{XX}$; L. V. = $^{5}/_{IX}$. The ophthalmometer showed R. 180° $44^{1}/_{2}$ 90° × $3^{1}/_{2}$; L. 180° $44^{1}/_{2}$ 00° × 1. She was put under homatropine gr. j ad ℥j, a drop to be put into each eye every fifteen minutes for two hours. At the end of that time the shadow-test gave: R., + 0.75, — 2.75; L. — 0.25, the examination being made with a plane mirror at a distance of one meter. I observed in this examination the appearance of the "internal shadows," much like the dark crescent of conical cornea, in the bright area of the pupil, to which I called attention some years ago and which I have found to vitiate very much the findings by this method of examination.

R. V. $=\frac{5}{XXV}$, with + 0.5 ⌒ — 2.75 180° $=\frac{5}{X}$; L. V. $=\frac{5}{VI}$, no glass improved. After the mydriatic effect had passed off: R. V.+=0.5 ⌒ — 2 180° $=\frac{5}{VI}$; L. — 0.5 $=\frac{5}{V}$. These were ordered. There had been no injury to either eye, nor was there any evidence of pathological change either interiorly or exteriorly to which the alteration in the corneal curve could be properly referred. There were no muscular anomalies, and the girl was in otherwise good health.

It will be seen from an examination of this history that there was an increase, in the course of six years, of a corneal astigmat sm of 2.5 D. in one eye and 0.75 D. in the other. There was also, apparently, a correcting lenticular astigmatism of 0.75 D. and 1 D. respectively. It is hardly possible that this could have been due to an error in observation, for at the first examination all the methods—subjective, ophthalmometer and skiascopy—practically agreed. The diminished visual acuteness found then is easily referable to the conjunctivitis. I will not pretend to assign any cause for the change in the corneal curvature which appears to be idiopathic, but would suggest that it is possibly due to a condition of the tissue similar to that leading to the development of conical cornea which usually manifests itself at about the age of the patient and of which it may be the beginning in this instance. A further study of the case, which I hope to be able to make, should throw some additional light upon this point.

EXOPHTHALMIC GOITRE ATTENDED BY RAPID INCREASE IN MYOPIA, OCCURRING IN AN ELDERLY SUBJECT.

BY CHAS. H. BEARD, M.D., CHICAGO, ILL.

THE patient in question, Mrs. S., from a neighboring town, a woman of unusual intelligence, and of great respectability, first consulted me September 3, 1895, though she had been known to me for several years previously. At the time of her first visit she was 61 years of age, hale, stout (weighing 175 to 180 pounds), looking and feeling well in every way. She was one of a large family of healthy children, several of

whom, both older and younger, are still living. She, however, had been considered the strong one of the family. Her only apparent bodily defect was myopia. This she thought she had always had, and it was with the view to a possible needed change in her glasses that she first came to me. She was the only one of the immediate family connection who was near-sighted. She was the mother of eight children, four of whom are living. None had eye trouble of any kind. The patient remembered that at the age of 18 years she wore glasses of the strength of $-\,{}^{1}/_{11}$ (about — 3.5 D.). At her first visit to me I found that her glasses were both — 4 D. Tests of her vision and refraction then resulted as follows:

R. E., V. = ${}^{10}/_{cc}$, ${}^{20}/_{xx}$ w. — 5 D.

L. E., V. = ${}^{10}/_{cc}$, ${}^{20}/_{xx}$ w. — 5 D.

For reading she required — 1 only. In all other respects her eyes were normal. Prescribed the above lenses in bifocal spectacles.

I heard nothing more from Mrs. S. for more than two years (December 9, 1897), when she came again to my office, having but lately come home after a sojourn in California. That, meanwhile, a tremendous change had occurred in her physical condition was evident from her striking appearance. She was emaciated in the extreme. Her last recorded weight had been 110 pounds, but she averred that since that she had been still further reduced until she could not have possessed over 100 pounds. The eyes were in a state of marked exophthalmos, with both the von Graefe and the Stellwag symptoms conspicuous. The pupils were normal excepting, perhaps, a little too large for one so old. Tests of vision and refraction now gave:

R. E., V. = ${}^{4}/_{cc}$, ${}^{20}/_{LXX}$ w. — 10 D.

L. E., V. = ${}^{6}/_{cc}$, ${}^{20}/_{xxx}$ w. — 6.5 D.

The ophthalmoscope verified as to these conditions, but showed no lesion. There were no coni about the optic discs. The media were all perfectly transparent. No ocular paralyses nor pareses. The ophthalmometer showed no astigmatism. There was no loss of function in any nerve of special sense.

She stated that all had gone well with her after her last visit for a few months, when she noticed a peculiar appearance of the nipple of the right mammary gland. She consulted her family physician, with whom I am personally acquainted, and

whom I know to be a man who stands high in the profession. He pronounced the trouble carcinoma, and in June, 1896, he removed the gland and adjacent lymphatics most thoroughly. None of her near relatives had been afflicted with carcinoma. Even in her case she had not been aware of an actual tumor or any swelling of the mamma, but merely of the retraction of the nipple. In the fall and early winter of 1896 she was in constant attendance upon her husband who was sick with carcinoma of the stomach. He died in December, 1896. Then she found herself greatly run down physically and was prevailed upon to go to Southern California, hoping to renew her strength. Her weight at this time was 165 pounds. After arriving in Pasadena her illness increased. She became the victim of an uncontrollable and persistent diarrhœa, and of a dreadful lassitude—she was always tired. She asserts that she lost weight at the rate of two pounds per week for eight months. She had insomnia; alternating polyuria, and scantiness—usually the latter; paroxysms of pyrexia, or at least of excessive heat. Throughout, however, her appetite remained good.

Dr. Norman Bridge, of Chicago and Pasadena, who made an examination of Mrs. S.'s case in the latter city May 5, 1897, has kindly furnished me with the following additional notes:

"*Patient has taken protonuclein almost constantly since the operation.*" (Referring to the excision of the mammary and lymphatic glands. I have taken the liberty of italicizing this sentence). "Weight now (three weeks ago) 148 pounds—January, 1897, 165 pounds. Weight when well 173 to 180 pounds. Took cold in head February 1, 1897. Head felt filled up. Still filled up. Mouth dry, full of slime in mornings. Smells, both sides, equally well. (Numbness in little and ring-finger after operation, and to present time). Since disappeared. Appetite good. Bowels loose rather than otherwise. Has taken powders occasionally of calomel and rhubarb, āā gr. ijss, and cinnamon, gr. j. Feels weak. Knees give out occasionally on rising a step, etc. Quadriceps extensors weak. Can not rise from a low chair without the aid of her hands. Knee-jerks excessive, ankle-clonus slight—right. Tremor of all four limbs on motion; face also—intention tremor. Still when at rest. No nystagmus. Is more nervous, not irritable. The trembling

makes her desirous of getting away by herself—at times. No headache. Says weakness has developed rapidly in the last three weeks, *i. e.*, on rising, also on standing, kneesmay tremble—"a giving-away" sensation. No urine symptoms, save scantiness at times. No albumen; no sugar."

She had never suffered from dyspnœa nor palpitations, though her pulse was rapid; and there was slight enlargement of the thyroid, more marked in the right lobe. Examination of the urine was negative. As the patient expressed herself as feeling very much better—only weak—I simply gave her stronger minus glasses and allowed her to go home.

On October 31, 1898, she came back again, declaring that she could no longer see so well with her glasses at a distance. In the interim her general health had vastly improved. She weighed probably about 130 pounds. The exophthalmus, however, notwithstanding the increased fullness of the face, was just as marked as ever. The pupils were still normal, excepting the possible slight dilatation. The intra-ocular tension was slightly lowered in both. Now:

R. E., V. = $^{2}/_{\infty}$, $^{20}/_{L}$ w. — 13 D.

L. E., V. = $^{4}/_{\infty}$, $^{20}/_{XXX}$ w. — 9 D.

The ophthalmoscope as yet revealed no lesion of retinæ or choroideæ. It may be that there was a tittle of pallor in the papillæ and a suspicion of smallness in the retinal vessels. The fields for white and colors were normal. It seemed that there had been further enlargement of the right lobe of the thyroid gland, but as to this I could not be positive. There was no pulsation visible in the retinal vessels and no bruit could be detected in the orbits. The heart-sounds were normal, but there was a pulse of 110 shortly after coming in from a gentle walk and no climbing, and of 96 after sitting quietly for three-quarters of an hour, though perfectly regular. On further questioning as to the patient's family history, it was ascertained that her eldest sister and her (the patient's) eldest daughter had goitres, though the doughter's was very slight. There was still no paralysis, and the other special senses were all perfect. Mrs. S. had never suffered any traumatism. Unfortunately, I have not tested the patient as to her electrical resistance. I found that the carotids were quite tense, and Mrs. S. informed me that fifteen years before, while working

over a very hot stove, on a very hot day, canning fruit, she suddenly lost the use of her right arm, but that within an hour or two it recovered; and that three years ago there had come a subconjunctival ecchymosis, but is not sure as to which eye was affected. I have not dared to use a cycloplegic in this case for fear of the effect on the choroidal and retinal circulation, but am convinced, from the various other tests and from the activity of the accommodation for one at her age, that the myopia is not simulative. Repeated examinations of the urine, both microscopic and reactionary, have failed to discover any abnormalities.

At the patient's last visit, December 19, 1898, the various conditions were unchanged, save that the general health was steadily growing better, and her weight, as last recorded, was 140 pounds. The tension of the globes, too, at this visit, was more nearly normal—it may be—quite so.

This case, to me, has been one of exceeding interest. Here we have, practically, every symptom of exophthalmic goitre, both major and minor, suddenly developed in an individual past 60 years of age; and, simultaneously, a remarkable increase in the previously existing myopia, amounting in the right eye to eight or nine dioptries, and in the left to four or five. This phenomenon has a number of times been mentioned in ophthalmic literature as occurring in conjunction with diabetes mellitus. Never, however, was there, in this case, a trace of sugar found in the urine, although it was repeatedly examined—first, by her family physician, then by Dr. Bridge, and lastly for me by Dr. Brougham, Pathologist to the Passavant Memorial Hospital. Even had there been, at any time, glycosuria present, the fact, taken together with the other conditions, would only have served to emphasize the theory of ophthalmic goitre, since it has been established not only that excretion of sugar by the kidneys is easily brought about in patients suffering from Basedow's disease (Meynert's and Chvastek's clinics were able to produce alimentary glycosuria with great facility in patients who had Graves disease ["Sajou's Annual," Vol. II, page 491]), but that it is not an infrequent symptom. These facts have led me to wonder if some of the cases reported of sudden and rapid increase in, or development of myopia, as accompanying diabetes may not have really been in relation to obscure exophthalmic goitre with glycosu-

ria. In view of the comparatively little that is known of the pathology of the two diseases such would seem more relevant.

Reverting to the case here in question, it has occurred to me since receiving the *hint* contained in Dr. Bridge's report, that it is not unlikely that the continued ingestion of protonuclein might here afford a possible clue as to the causation. This substance is said to be a combination of animal extracts. Among those who have made special study of the physiological effects of the thyroid extract, for example, it is pretty well agreed that its administration would be decidedly contraindicated in cases where there existed an enlargement of the thyroid gland. A *tendency* to goitre might also furnish an incompatibility. Fuhthermore, the query arises, are we prepared, authoritatively, to deny that even others like the so-called lymphoid and other glandular extracts may not, in certain pre-existing dystrophies, yet further disturb the metabolic forces and lead to grave consequences? The time is drawing near, no doubt, when the influences exerted by these compounds—the toxins, etc., on the animal economy will be comparatively clear to the medical mind; at present, in addition to being highly subtle, their action is profoundly obscure

In justice to the physician who prescribed the remedy in this instance, let me add that his action in the matter was absolutely above reproach, even granting that the above extremely vague surmises could be substantiated. He was only following the popular teaching of the day. Yes, better than that, for in proof of his foresight and caution, he actually questioned and examined the patient with regard to an enlarged thyroid and decided, before giving the treatment, that there was none. Had the contrary been not only true, but most apparent, he would still have had warrant for what he did; for, while I stated above that it was pretty well agreed as to the harmful effects of the thyroid extract in exophthalmic goitre, I am perfectly aware that some men of eminence have advocated its use in this very affection, and, moreover, have reported series of cases as benefited thereby.

In conclusion, I wish to state that I report this case solely on account of the two things mentioned in the heading, which struck me might interest my colleagues, and these later remote conjectures are wholly secondary.

MEDICAL SOCIETIES.

FOURTH ANNUAL MEETING OF THE WESTERN OPHTHALMOLOGICAL AND OTO LARYNGOLOGICAL ASSOCIATION.

In spite of the cold weather and obstacles of travel in consequence of this, the meeting of the Western Ophthalmological and Oto-Laryngological Association, held on February 10 and 11, in New Orleans, La., was very well attended. The scientific work was interesting and instructive.

Dr. G. T. Stevens' excellent address was of unusual interest and highly appreciated.

The social features through the well-known hospitality of the citizens of the Southern Metropolis were most enjoyable.

The following officers were elected:

W. Scheppegrell, New Orleans, President.

Dr. M. A. Goldstein, St. Louis, Dr. Casey A. Wood, Chicago, Dr. E. C. Ellett, Memphis, Vice-Presidents.

Dr. F. C. Ewing, St. Louis, Secretary.

Dr. W. L. Dayton, Lincoln, Neb., Treasurer.

The next meeting will be held in St. Louis on the second Thursday, Friday and Saturday in April, 1900.

AMERICAN MEDICAL ASSOCIATION—SECTIONS ON OPHTHALMOLOGY, AND LARYNGOLOGY AND OTOLOGY.

At the June meeting of the American Medical Association at Columbus, Ohio, in addition to their regular programs, the Section on Ophthalmology and that of Laryngology and Otology, will devote the morning of the second day, June 7, to a joint meeting, under the chairmanship of Dr. Casey A. Wood, of Chicago, and of Dr. Emil Mayer, of New York.

The subject for discussion will be "The Relation of Ocular Diseases to Affections of the Nose and Neighboring Cavities."

Four papers will be read on this subject, by invitation, as follows:

1. Dr. Charles Stedman Bull, of New York, "Some Points in the Symptomatology, Pathology and Treatment of the Sinuses Adjacent and Accessory to the Orbit."

2. Dr. D. Bryson Delevan, of New York, "Nasal Stenosis in their Relation to the Ocular Disturbances."

3. Dr. Joleph A. White, of Richmond, Va., "Eye Troubles Attributable to Naso-Pharyngeal and Aural Disturbances."

4. Dr. J. H. Bryan, of Washington, D. C., "Diseases of the Accessory Sinuses in Their Relation to Diseases of the Eye."

5. General discussion on the main question.

PAMPHLETS RECEIVED.

"Further Report on Xeroform in Ocular Therapeutics," by B. Wicherkiewicz, M.D.

"Some Remarks About the Study of Medicine in Germany," by E. Amberg, M.D.

"Some New Throat Instruments, With indications for Their Use," by G. H. Makuen, M.D.

"On Continuous Sterilization for Knives and Other Cutting Instruments," by J. A. Lippincott, M.D.

"Thrombosis of the Lateral Sinus, Dependent Upon Suppurative Otitis Media," by E. B. Dench, M.D.

"Radical Cure of Inguinal Hernia by Fowler's Method, With Reports of Cases," by H. O. Walker, M.D.

"Infective Intracranial Complications of Aural Disease,—Diagnosis and Treatment," by A. Timberman, M.D.

"Removal of the Tarsus and Retrotarsal Folds in Certain Cases of Chronic Trachoma," by C. A. Wood, M.D.

"Further Observations Regarding the Use of the Bone-Clamp in Ununited Fractures, Etc." by Cl. Parkhill, M.D.

"The Phonendoscope and Its Practical Application." Lectures by Aurelio Bianchi, M.D., F. Regnault, M.D., and M. Anastasiades, M.D. Translated by A. G. Baker, M.D.